

BEST AVAILABLE COPY

Serial No. 10/754,923

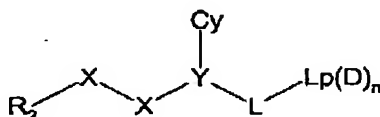
Response to Office Action of November 26, 2004

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1 (previously presented): A serine protease inhibitor compound of formula (I)



(I)

wherein:

R<sub>2</sub> is:-

(i) phenyl optionally being substituted in the 3 and/or 4 position by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, MeSO<sub>2</sub>- or R<sub>1</sub>, and optionally substituted at the 6 position by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio;

(ii) naphth-2-yl optionally substituted at the 6 or 7 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>; and optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio;

(iii) isoquinolin-7-yl, indol-5-yl, indol-6-yl, indazol-5-yl, indazol-6-yl, benzothiazol-6-yl or benzisoxazol-5-yl optionally substituted at the 3 position by halo, haloalkoxy,

Serial No. 10/754,923

Response to Office Action of November 26, 2004

haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1j</sub>;

(iv) benzimidazol-5-yl or benzothiazol-6-yl optionally substituted at the 2 position by amino;

(v) thien-2-yl or thien-3-yl optionally substituted at the 4 or 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(vi) 3,4-methylenedioxyphenyl, 2,3-dihydroindol-6-yl, 3,3-dichloro-2-oxo-indol-6-yl or 1-methyl-3-aminoindazol-5-yl;

(vii) benzothiazol-2-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydroimidazo[1,2-a]pyrimidin-2-yl;

(viii) pyrazol-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(ix) pyrid-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(x) pyrid-3-yl optionally substituted at the 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(xi) benzofur-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1j</sub>;

(xii) indol-2-yl optionally substituted on the indole nitrogen atom by alkyl and optionally substituted at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1j</sub>;

(xiii) indol-6-yl substituted at the 5 position by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio and optionally substituted at

Serial No. 10/754,923

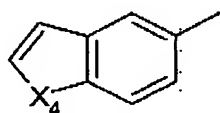
Response to Office Action of November 26, 2004

the 3 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ; or

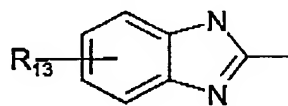
(xiv) benzo[b]thiophen-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ;

with the proviso that  $R_2$  cannot be aminoisoquinolyl;

or  $R_2$  is a group of formula (F') or (H')



(F')



(H')

wherein  $X_4$  is O or S, and  $R_{13}$  is selected from hydrogen, fluoro, chloro and methyl;

-X-X- is -CONH-;

$R_1$  is hydrogen, hydroxy, alkoxy, alkyl, alkylaminoalkyl, alkanoyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkylamino, carboxyl, carboxymethyl, amido or amidomethyl;

$R_{1j}$  is hydrogen, hydroxy, alkoxy, alkyl, alkanoyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylamino, carboxyl, carboxymethyl, amido or amidomethyl;

Y (the  $\alpha$ -atom) is a CH group;

Cy is an optionally  $R_{3a}$  substituted: phenyl, pyridyl, thienyl, thiazolyl, naphthyl, piperidinyl, furanyl, pyrrolyl, isoxazolyl, isothiazolyl; pyrazolyl, oxazolyl, imidazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, pyrimidinyl, pyridazinyl, quinolyl, isoquinolyl, benzofuryl, benzothienyl or cycloalkyl group, or a phenyl group substituted by  $R_{3i}X_1$ ;

Serial No. 10/754,923

Response to Office Action of November 26, 2004

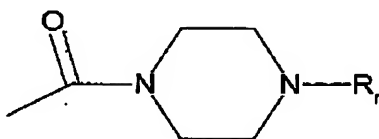
each  $R_{3a}$  independently is hydrogen, hydroxyl, alkoxy, aralkyloxy, alkyl, alkylaminoalkyl, hydroxymethyl, carboxy, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, aminomethyl,  $CONH_2$ ,  $CH_2CONH_2$ , (1-6C)alkanoylamino, alkoxycarbonylamino, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkylimidazolyl, thiazolyl, alkylthiazolyl, alkyloxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy, haloalkyl, a group of the formula  $-C(X^3)N(R^{11})R^{12}$  (wherein  $X^3$  is O or S; and  $R^{11}$  and  $R^{12}$  are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group), or  $-OCH_2O-$  which is bonded to two adjacent ring atoms in Cy;

$X_1$  is a bond, O, NH or  $CH_2$ ;

$R_{3i}$  is phenyl, pyridyl or pyrimidinyl optionally substituted by  $R_{3a}$ ;

and

$-L-Lp(D)_n$  is of the formula:



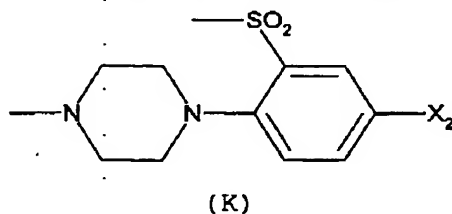
in which  $R_f$  is  $-(CH_2)_c-R_c$ ,  $-CHReR_f$ ,  $-CH_2-CHReR_f$ ,  $-CH_2-CH_2-CHReR_f$ , or  $R_g$  in which  $c$  is 1 or 2;  $R_c$  is thienyl, thiazolyl (which may bear an amino substituent), isothiazolyl, oxazolyl, isoxazolyl, pyrazolyl, imidazolyl, pyridyl (which may bear an alkylsulphonyl, aminosulphonyl, alkylaminosulphonyl, alkylaminocarbonyl, amino, amido, (1-4C)alkoxycarbonyl, carboxy, acetylamino, chloro, fluoro, cyano, (1-3C)alkyl, trifluoromethyl, methoxy, ethoxy, nitro, hydroxy, alkylsulphonylamino, triazolyl or tetrazolyl substituent), pyrimidinyl, pyridazinyl, pyrazinyl or phenyl

Serial No. 10/754,923

Response to Office Action of November 26, 2004

(which may bear a methyl, methylamino, dimethylamino, carboxy, dialkylaminosulphonyl, alkylsulphonyl, aminosulphonyl, alkylaminosulphonyl, alkylaminocarbonyl, amino, amido, alkoxy, acetyl, chloro, fluoro, cyano, methoxy, ethoxy, nitro, hydroxy, alkylsulphonylamino, triazolyl or tetrazolyl substituent); each of  $R_e$  and  $R_f$  independently is hydrogen or  $C_{1-3}$ alkyl; or  $CH(R_e)R_f$  is cyclopentyl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 3- or 4-position), cyclohexyl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 3- or 4-position), tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, pyrrolidin-3-yl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 1-position), piperidin-4-yl (which may bear a hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl or ethoxycarbonyl substituent at the 1-position), or indan-2-yl; and  $R_g$  is 2-methylsulphonylphenyl which may bear a 4-fluoro substituent or  $R_g$  is  $\lambda^6$ -1,1-dioxobenzo[b]thiophen-7-yl;

or a physiologically-tolerable salt thereof;  
provided that  $Lp(D)n$  is not of the formula (K):



wherein  $X_2$  is fluoro or hydrogen.

2 (previously presented): A compound according to claim 1

Serial No. 10/754,923

Response to Office Action of November 26, 2004

wherein:

R<sub>2</sub> is:-

(i) phenyl optionally being substituted in the 3 and/or 4 position by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, MeSO<sub>2</sub>- or R<sub>1</sub>, and optionally substituted at the 6 position by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio;

(ii) naphth-2-yl optionally substituted at the 6 or 7 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>; and optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio;

(iii) isoquinolin-7-yl, indol-5-yl, indol-6-yl, indazol-5-yl, indazol-6-yl, benzothiazol-6-yl or benzisoxazol-5-yl optionally substituted at the 3 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(iv) benzimidazol-5-yl or benzothiazol-6-yl optionally substituted at the 2 position by amino;

(v) thien-2-yl or thien-3-yl optionally substituted at the 4 or 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

(vi) 3,4-methylenedioxyphenyl, 2,3-dihydroindol-6-yl, 3,3-dichloro-2-oxo-indol-6-yl or 1-methyl-3-aminoindazol-5-yl;

(vii) benzothiazol-2-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydroimidazo[1,2-a]pyrimidin-2-yl;

(viii) pyrazol-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;

Serial No. 10/754,923

Response to Office Action of November 26, 2004

(ix) pyrid-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_1$ ;

(x) pyrid-3-yl optionally substituted at the 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_1$ ;

(xi) benzofur-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ;

(xii) indol-2-yl optionally substituted on the indole nitrogen atom by alkyl and optionally substituted at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ;

(xiii) indol-6-yl substituted at the 5 position by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio and optionally substituted at the 3 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ; or

(xiv) benzo[b]thiophen-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ;

with the proviso that  $R_2$  cannot be aminoisoquinolyl;

Cy is an optionally  $R_{3a}$  substituted: phenyl, pyridyl, thienyl, thiazolyl, naphthyl, piperidinyl or cycloalkyl group;

each  $R_{3a}$  independently is hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, methylaminomethyl, dimethylaminomethyl, hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl,

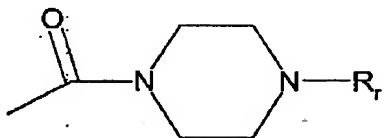
Serial No. 10/754,923

Response to Office Action of November 26, 2004

aminomethyl,  $\text{CONH}_2$ ,  $\text{CH}_2\text{CONH}_2$ , acetamino, methoxycarbonylamino, ethoxycarbonylamino, t-butoxycarbonylamino, amino, fluoro, chloro, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, methylsulphenyl, methylsulphonylamido, ethylsulphonylamido, methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl, trifluoromethoxy or trifluoromethyl;

and

-L-Lp(D)<sub>n</sub> is of the formula:



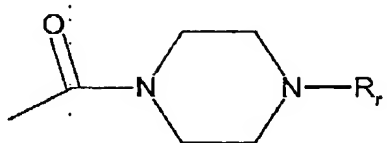
in which  $\text{R}_f$  is  $-(\text{CH}_2)_c-\text{R}_c$ ,  $-\text{CHR}_e\text{R}_f$ ,  $-\text{CH}_2-\text{CHR}_e\text{R}_f$ , or  $\text{R}_g$  in which  $c$  is 1 or 2;  $\text{R}_c$  is pyridyl or phenyl (which phenyl may bear a fluoro, chloro, methyl,  $\text{CONH}_2$ ,  $\text{SO}_2\text{NH}_2$ , methylaminosulphonyl, dimethylaminosulphonyl, methoxy or methylsulphonyl substituent); each of  $\text{R}_e$  and  $\text{R}_f$  independently is hydrogen or  $\text{C}_{1-3}$ alkyl; or  $\text{CHR}_e\text{R}_f$  is cyclopentyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position), cyclohexyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position), tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, pyrrolidin-3-yl (which may bear a 1-methyl substituent), piperidin-4-yl (which may bear a 1-methyl substituent) or indan-2-yl; and  $\text{R}_g$  is 2-methylsulphonylphenyl which may bear a 4-fluoro substituent or  $\text{R}_g$  is  $\lambda^6$ -1,1-dioxobenzo[b]thiophen-7-yl.

3 (original): A compound according to claim 1 wherein -L-Lp(D)<sub>n</sub> is of the formula:



Serial No. 10/754,923

Response to Office Action of November 26, 2004



in which R<sub>R</sub> is -(CH<sub>2</sub>)<sub>c</sub>-R<sub>C</sub>; in which c is 2; R<sub>C</sub> is thienyl, thiazolyl (which may bear an amino substituent), isothiazolyl, oxazolyl, isoxazolyl, pyrazolyl, imidazolyl, pyridyl (which may bear an amino, methoxycarbonyl, carboxy, fluoro, cyano, methyl, methylsulphonyl, aminosulphonyl, methylaminosulfonyl, dimethylaminosulfonyl, or trifluoromethyl substituent), pyrimidinyl, pyridazinyl, pyrazinyl or phenyl (which phenyl may bear a fluoro, chloro, cyano, methyl, amino, methylsulphonyl, aminosulphonyl, methylaminosulphonyl, dimethylaminosulphonyl, methylamino, dimethylamino, carboxy, methoxycarbonyl or methoxy substituent).

4 (previously presented): A compound according to claim 3 wherein R<sub>C</sub> is thiazolyl (which may bear an amino substituent), pyrimidinyl, pyrazolyl, imidazolyl, pyridyl (which may bear a methylsulphonyl, aminosulphonyl, methylaminosulfonyl, dimethylaminosulfonyl, fluoro, cyano, methyl or trifluoromethyl substituent), pyridazinyl, pyrazinyl or phenyl (which phenyl may bear a fluoro, chloro, cyano, methyl, amino, methylamino, dimethylamino, carboxy, methoxycarbonyl, methylsulphonyl, aminosulphonyl, methylaminosulfonyl, dimethylaminosulfonyl, or methoxy substituent).

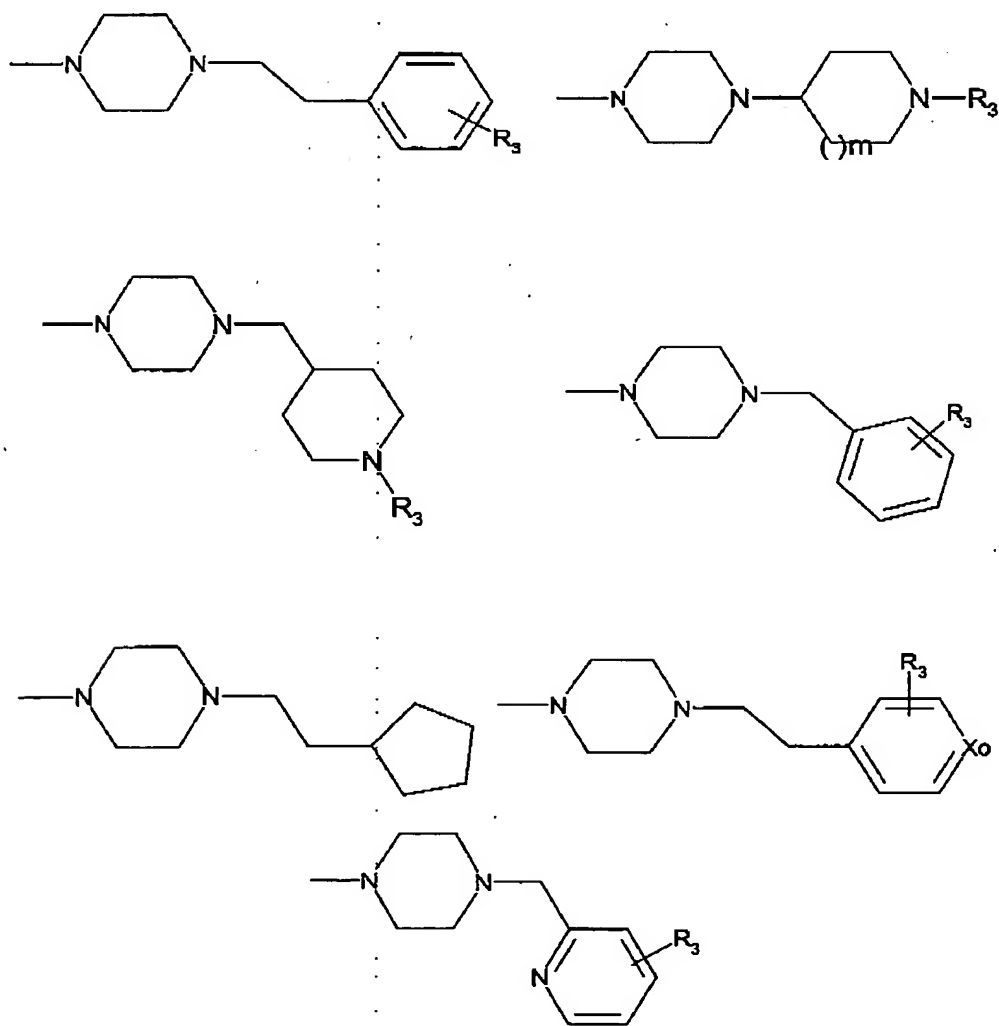
5 (previously presented): A compound according to claim 4 wherein R<sub>C</sub> is thiazolyl (which may bear an amino substituent), pyrazolyl, imidazolyl, pyridyl (which may bear a fluoro, cyano, methyl or trifluoromethyl substituent), pyridazinyl or pyrazinyl.

Serial No. 10/754,923

Response to Office Action of November 26, 2004

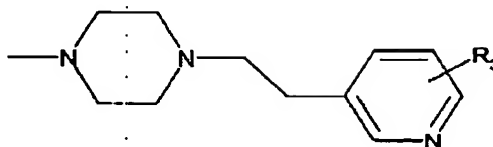
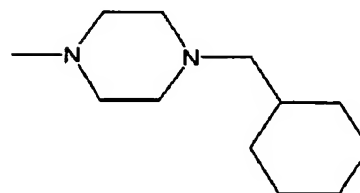
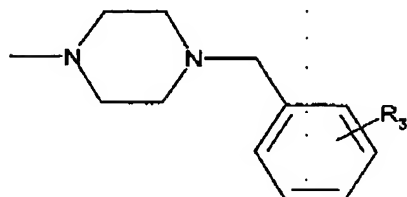
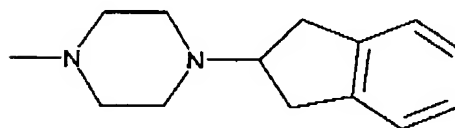
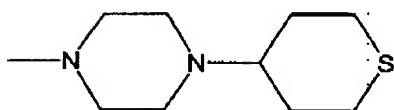
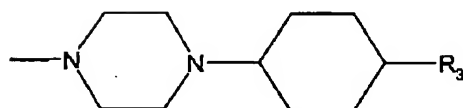
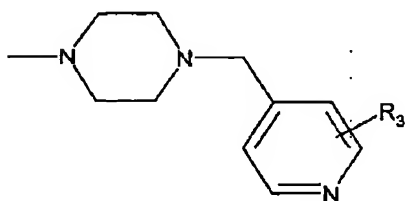
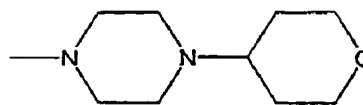
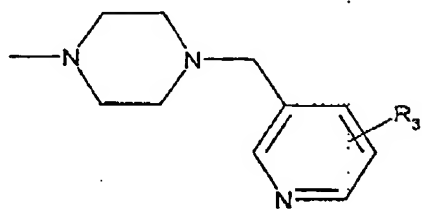
6 (previously presented): A compound according to claim 5 wherein  $R_c$  is thiazol-2-yl, 2-aminothiazol-4-yl, pyrazol-1-yl, pyrazol-4-yl, pyridazin-3-yl, imidazol-1-yl, imidazol-4-yl, pyrazin-2-yl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, 3-fluoropyrid-4-yl, 2-cyanopyrid-4-yl, 2-methylpyrid-4-yl or 2-trifluoromethylpyrid-6-yl.

7 (currently amended): A compound according to claim 1 wherein  $L$  is CO and  $-Lp(D)_n$  is of the formula:



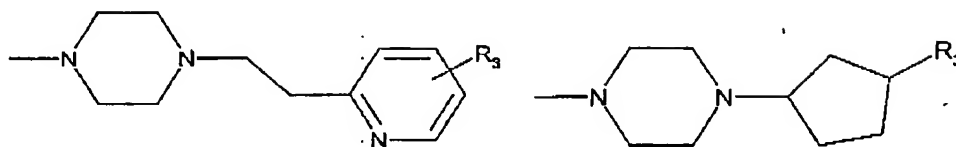
Serial No. 10/754,923

Response to Office Action of November 26, 2004



Serial No. 10/754,923

Response to Office Action of November 26, 2004



wherein;

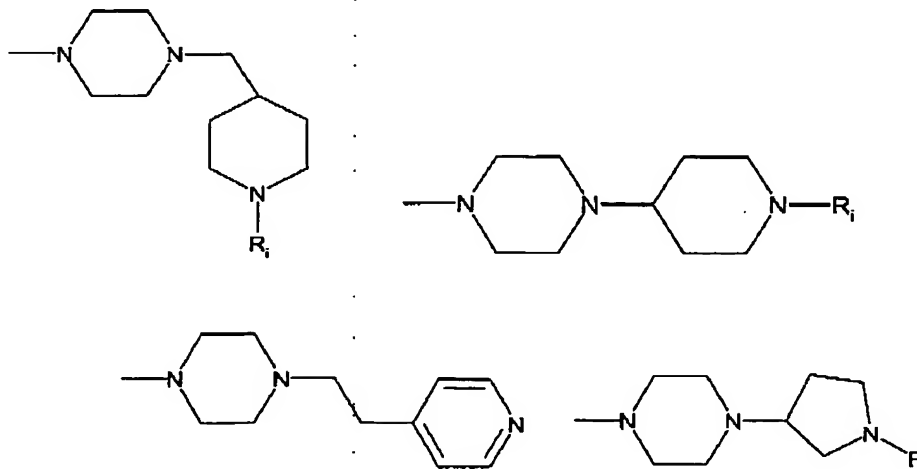
m represents 0 or 1;

 $Xo \text{ } x^{\theta}$  represents CH or N; and

when  $R_3$  is present as a substituent on an aromatic ring, it is selected from hydrogen, alkylsulphonyl, aminosulphonyl, alkylaminosulphonyl, alkylaminocarbonyl, amino, amido, alkoxycarbonyl, acetyl amino, chloro, fluoro, cyano, methoxy, ethoxy, nitro, hydroxy, alkylsulphonylamino, triazolyl and tetrazolyl; and

when  $R_3$  is present as a substituent on a saturated ring, it is selected from hydrogen, hydroxy, amino, (1-3C)alkoxy, (1-3C)hydroxyalkyl, (1-3C)alkyl, carboxy, methoxycarbonyl and ethoxycarbonyl.

8 (currently amended): A compound according to claim 7 wherein -Lp(D)n is of the formula:



wherein  $R_1$  is hydrogen, methyl or ethyl or ~~(1-6C)alkyl~~.

Serial No. 10/754,923

Response to Office Action of November 26, 2004

9 (previously presented): A compound according to claim 1 wherein R<sub>2</sub> is:-

(i) phenyl optionally being substituted in the 3 and/or 4 position by fluoro, chloro, bromo, iodo, nitro, difluoromethoxy, trifluoromethoxy, amino, cyano, trifluoromethyl, methylthio, vinyl, carboxy, acetoxy, MeSO<sub>2</sub>-, hydroxy, methoxy, ethoxy, methyl, methoxycarbonyl, methylamino, ethylamino or amido, and optionally substituted at the 6 position by amino, hydroxy, fluoro, methoxycarbonyl, cyano or aminomethyl;

(ii) naphth-2-yl optionally substituted at the 6, position by hydroxy and optionally substituted at the 3 position by amino or hydroxy;

(iii) isoquinolin-7-yl, indol-5-yl, indol-6-yl, indazol-5-yl, indazol-6-yl, benzothiazol-6-yl or benzisoxazol-5-yl optionally substituted at the 3 position by chloro, bromo, amino, methyl or methoxy;

(iv) benzimidazol-5-yl or benzothiazol-6-yl optionally substituted at the 2 position by amino;

(v) thien-2-yl or thien-3-yl optionally substituted at the 4 or 5 position by methylthio, methyl or acetyl;

(vi) 3,4-methylenedioxyphenyl, 2,3-dihydroindol-6-yl, 3,3-dichloro-2-oxo-indol-6-yl or 1-methyl-3-aminoindazol-5-yl;

(vii) benzothiazol-2-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydroimidazo[1,2-a]pyrimidin-2-yl;

(viii) pyrazol-2-yl substituted at the 5 position by methyl;

(ix) 5-chloropyrid-2-yl;

(x) pyrid-3-yl or 6-chloropyrid-3-yl;

(xi) benzofur-2-yl, 5-chlorobenzofur-2-yl, 3-methylbenzofur-2-yl, 5-methylbenzofur-2-yl or 6-methoxybenzofur-2-yl; (xii) indol-2-yl optionally substituted on the indole nitrogen atom by methyl and optionally

Serial No. 10/754,923

Response to Office Action of November 26, 2004

substituted at the 5 or 6 position by fluoro, chloro, bromo, methyl or methoxy;

(xiii) indol-6-yl substituted at the 5 position by chloro, fluoro or hydroxy and optionally substituted at the 3 position by chloro or methyl; or

(xiv) benzo[b]thiophen-2-yl optionally substituted at the 3 position by fluoro, chloro or methyl, and optionally substituted at the 5 or 6 position by fluoro, chloro, methyl, hydroxy, or methoxy.

10 (previously presented): A compound according to claim 9 wherein R<sub>2</sub> is:-

(i) phenyl, 2-aminophenyl, 3-aminophenyl, 2-amino-4-fluorophenyl, 2-amino-4-chlorophenyl, 2-amino-4-nitrophenyl, 2-amino-4-methylphenyl, 3,4-diaminophenyl, 3-amino-4-fluorophenyl, 3-amino-4-chlorophenyl, 3-amino-4-bromophenyl, 3-amino-4-hydroxyphenyl, 3-amino-4-carboxymethylphenyl, 3-amino-4-methylphenyl, 3-amino-4-methoxyphenyl, 2-fluorophenyl, 4-fluoro-3-cyanophenyl, 3-chlorophenyl, 3-chloro-4-hydroxyphenyl, 4-chlorophenyl, 4-chloro-2-hydroxyphenyl, 4-chloro-3-hydroxyphenyl, 4-chloro-3-methylphenyl, 4-chloro-3-methoxyphenyl, 4-bromophenyl, 4-bromo-3-methylphenyl, 4-iodophenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, 2-hydroxyphenyl, 2-hydroxy-4-methoxyphenyl, 3-hydroxyphenyl, 3-hydroxy-4-methylphenyl, 2,4-dihydroxyphenyl, 3,4-dihydroxyphenyl, 3-hydroxy-4-methoxyphenyl, 4-difluoromethoxyphenyl, 4-trifluoromethoxyphenyl, 4-trifluoromethylphenyl, 4-methylthiophenyl, 4-methoxycarbonylphenyl, 4-acetoxyphenyl, 4-methanesulfonylphenyl, 3-methylphenyl, 4-methylphenyl, 4-vinylphenyl, 4-methoxyphenyl, 4-ethoxyphenyl, 4-methoxy-3-chlorophenyl, 4-methoxy-3-methylphenyl, 3-methylaminophenyl, 4-methylaminophenyl, 4-ethylaminophenyl or 2-aminomethylphenyl;

Serial No. 10/754,923

Response to Office Action of November 26, 2004

(ii) naphth-2-yl, 3-aminonaphth-2-yl, 3-hydroxynaphth-2-yl or 6-hydroxynaphth-2-yl;

(iii) isoquinolin-7-yl, indol-5-yl, indol-6-yl, 3-chloroindol-6-yl, 3-bromoindol-6-yl, 3-methylindol-6-yl, 3-methoxyindol-6-yl, indazol-5-yl, 3-aminoindazol-5-yl, indazol-6-yl, benzothiazol-6-yl, 3-aminobenzisoxazol-5-yl;

(iv) benzimidazol-5-yl, 2-aminobenzimidazol-5-yl, or benzothiazol-6-yl;

(v) thien-2-yl, 5-methylthien-2-yl, 5-methylthio-thien-2-yl, 5-acetylthien-2-yl or thien-3-yl;

(vi) 3,4-methylenedioxyphenyl, 2,3-dihydroindol-6-yl, 3,3-dichloro-2-oxo-indol-6-yl or 1-methyl-3-aminoindazol-5-yl;

(vii) benzothiazol-2-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydroimidazo[1,2-a]pyrimidin-2-yl;

(viii) 5-methylpyrazol-2-yl;

(ix) 5-chloropyrid-2-yl;

(x) pyrid-3-yl, 6-chloropyrid-3-yl;

(xi) benzofur-2-yl, 5-chlorobenzofur-2-yl, 3-methylbenzofur-2-yl, 5-methylbenzofur-2-yl, 6-methoxybenzofur-2-yl;

(xii) indol-2-yl, 5-fluoroindol-2-yl, 5-chloroindol-2-yl, 5-methylindol-2-yl, 5-methoxyindol-2-yl, 6-methoxyindol-2-yl and 1-methyl-indol-2-yl;

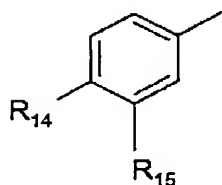
(xiii) 5-fluoroindol-6-yl; or

(xiv) benzo[b]thiophen-2-yl, 5-chloro- benzo[b]thiophen-2-yl or 6-chlorobenzo[b]thiophen-2-yl.

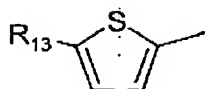
11 (previously presented): A compound according to claim 1 wherein R<sub>2</sub> is selected from one of the formula (A') to (H'):

Serial No. 10/754,923

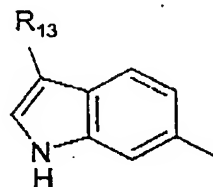
Response to Office Action of November 26, 2004



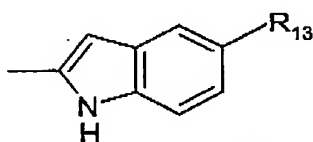
(A')



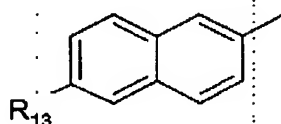
(B')



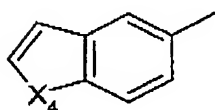
(C')



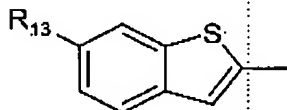
(D')



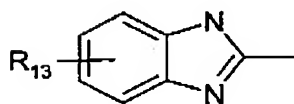
(E')



(F')



(G')



(H')

wherein  $X_4$  is O or S,  $R_{13}$  is selected from hydrogen, fluoro [except for (C')], chloro or methyl and  $R_{14}$  is selected from hydrogen, methyl, ethyl, fluoro, chloro, and methoxy and  $R_{15}$  is selected from hydrogen, methyl, fluoro, chloro and amino.

12 (previously presented): A compound according to claim 11, wherein  $R_2$  is 4-chlorophenyl, 4-methoxyphenyl, 3-amino-4-chlorophenyl, indol-2-yl, 5-chloroindol-2-yl, indol-6-yl, 3-chloroindol-6-yl or 3-methylindol-6-yl.



Serial No. 10/754,923

Response to Office Action of November 26, 2004

13 (canceled):

14 (canceled):

15 (canceled):

16 (canceled):

17 (canceled):

18 (canceled):

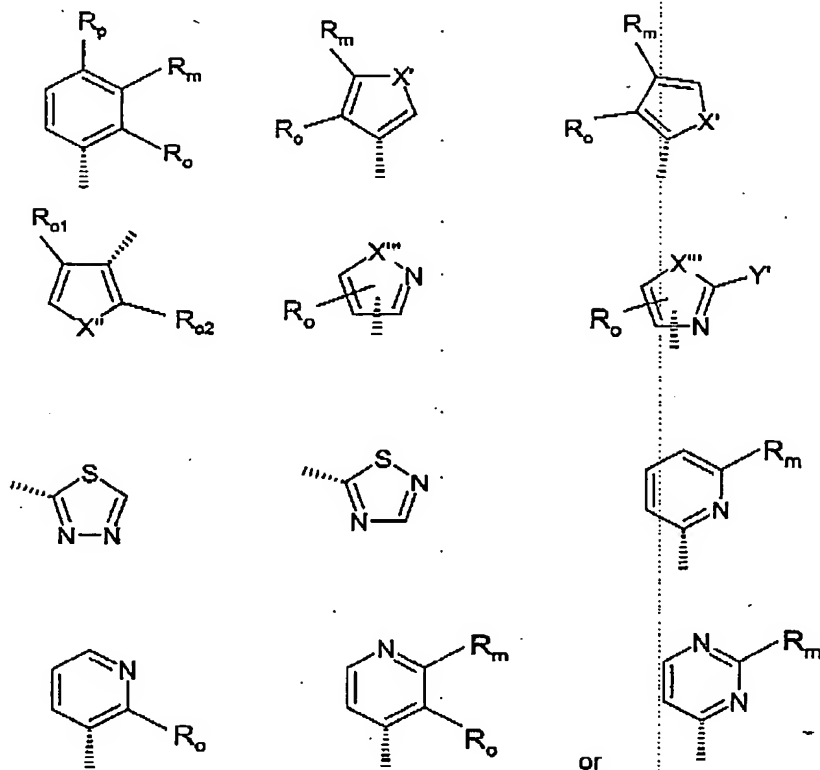
19 (previously presented): A compound according to claim 1 wherein R<sub>3a</sub> is selected from hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, methylaminomethyl, dimethylaminomethyl, hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl, aminomethyl, CONH<sub>2</sub>, CH<sub>2</sub>CONH<sub>2</sub>, acetylamino, methoxycarbonylamino, ethoxycarbonylamino, t-butoxycarbonylamino, amino, fluoro, chloro, bromo, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, methylsulphenyl, methylsulphonylamido, ethylsulphonylamido, methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl, trifluoromethoxy, trifluoromethyl, bromo, -OCH<sub>2</sub>O- (which is bonded to two adjacent ring atoms in Cy) and -C(X<sup>3</sup>)N(R<sup>11</sup>)R<sup>12</sup> (wherein X<sup>3</sup> is O or S and R<sup>11</sup> and R<sup>12</sup> are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group).

20 (canceled):

Serial No. 10/754,923

Response to Office Action of November 26, 2004

21 (previously presented): A compound according to claim 1  
wherein Cy is selected from:



wherein:

X' is selected from O, S and NMe;

X'' is selected from O and S;

X''' is selected from O, S, NH and NMe;

Y' is selected from hydrogen, amino and methyl;

R<sub>0</sub> is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphinyl and methylsulphonyl;

R<sub>m</sub> is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphinyl, methylsulphonyl, carboxy, methoxycarbonyl and a group of the

Serial No. 10/754,923

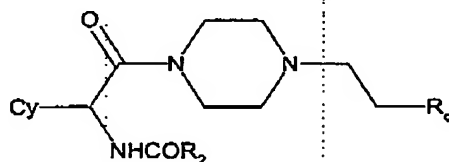
Response to Office Action of November 26, 2004

formula  $-C(X^3)N(R^{11})R^{12}$  (wherein  $X^3$  is O or S and  $R^{11}$  and  $R^{12}$  are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group);  $R_p$  is selected from hydrogen and fluoro; or  $R_o$  and  $R_m$  or  $R_m$  and  $R_p$  form an  $-OCH_2O-$  group; or  $R_o$  and  $R_m$  together with the ring to which they are attached form a 5 or 6 membered aryl or heteroaryl ring (wherein the heteroaryl ring contains 1 or 2 heteroatoms selected from nitrogen, oxygen and sulfur); and

one of  $R_{O1}$  and  $R_{O2}$  is hydrogen and the other is  $R_o$ .

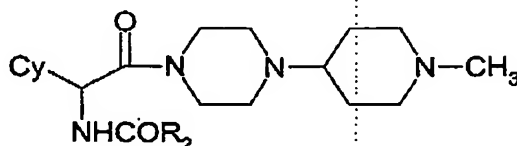
22 (previously presented): A compound according to claim 1 wherein Cy is selected from phenyl, 2-chlorophenyl, 2-methoxyphenyl, 4-carbamoylphenyl, pyrid-2-yl, pyrid-4-yl, thien-2-yl, thien-3-yl, furan-2-yl, furan-3-yl, imidazol-2-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl and quinolin-4-yl.

23 (previously presented): A compound of the formula:



wherein Cy, R<sub>2</sub> and R<sub>6</sub> are as defined in any one of claims 1 to 6, 9 to 12, 19 and 21 to 22.

24 (previously presented): A compound of the formula:



Serial No. 10/754,923

Response to Office Action of November 26, 2004

wherein Cy and R<sub>2</sub> are as defined in any one of claims 1 to 2, 9 to 12, 19 and 21 to 22.

25 (canceled):

26 (previously presented): A compound as claimed in Claim 1, which is selected from:

1-(Indole-6-carbonyl-D-phenylglyciny1)-4-[2-(4-pyridinyl)-ethyl]piperazine;

1-(3-Chloroindole-6-carbonyl-D-phenylglyciny1)-4-[2-(4-pyridinyl)ethyl]piperazine;

1-(4-Methoxybenzoyl-D-phenylglyciny1)-4-(1-methylpiperidin-4-yl)piperazine;

1-(4-Methoxybenzoyl-D-(2-chlorophenyl)glyciny1)-4-(1-methylpiperidin-4-yl)piperazine;

1-(Indole-6-carbonyl-D-(2-chlorophenyl)glyciny1)-4-(1-methylpiperidin-4-yl)piperazine; and

1-(4-Methoxybenzoyl-D-(2-trifluoromethylphenyl)glyciny1)-4-(1-methylpiperidin-4-yl)piperazine;

and physiologically-tolerable salts thereof.

27 (previously presented): A pharmaceutical composition, which comprises a compound as claimed in claim 1 together with at least one pharmaceutically acceptable carrier or excipient.

28 (canceled):

29 (canceled):

30 (previously presented): A method of treatment of a human or non-human animal body to combat a thrombotic disorder selected from venous thrombosis, pulmonary embolism, arterial thrombosis, myocardial ischaemia, myocardial infarction and

Serial No. 10/754,923

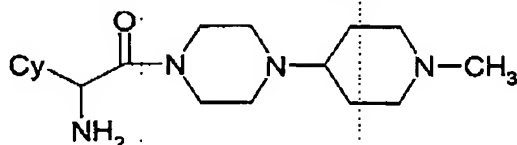
Response to Office Action of November 26, 2004

cerebral thrombosis, which comprises administering to said body an effective amount of a compound as claimed in claim 1.

31 (canceled):

32 (canceled):

33 (previously presented): A compound of the formula



or a salt thereof in which Cy is as defined in any one of claims 1, 21 and 22.

34 (previously presented): A compound as claimed in any one of claims 1 to ~~12-13~~, 19 and 21 to 22, wherein the alpha atom in Y ~~is carbon and~~ has the conformation that would result from construction from a D- $\alpha$ -amino acid NH<sub>2</sub>-CH(Cy)-COOH where the NH<sub>2</sub> represents part of X-X.

35 (previously presented): A pharmaceutical composition, which comprises a compound as claimed in claim 34 together with at least one pharmaceutically acceptable carrier or excipient.

36 (previously presented): A method of treatment of a human or non-human animal body to combat a thrombotic disorder selected from venous thrombosis, pulmonary embolism, arterial thrombosis, myocardial ischaemia, myocardial infarction and cerebral thrombosis, which comprises administering to said body an effective amount of a compound as claimed in claim 34.

37 (previously presented): A method as claimed in claim 36 in which said human or non-human animal body is a human body.

Serial No. 10/754,923

Response to Office Action of November 26, 2004

38 (new) A compound as claimed in claim 33, in which the carbon atom bearing Cy has the conformation that would result from construction from a D- $\alpha$ -aminoacid  $\text{NH}_2\text{-CH}(\text{Cy})\text{-COOH}$ .

39 (new) A compound as claimed in claim 38, in which Cy is a phenyl group.

**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record**

**BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

☐ BLACK BORDERS

☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES

☐ FADED TEXT OR DRAWING

☒ BLURRED OR ILLEGIBLE TEXT OR DRAWING

☐ SKEWED/SLANTED IMAGES

☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS

☐ GRAY SCALE DOCUMENTS

☐ LINES OR MARKS ON ORIGINAL DOCUMENT

☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY

☐ OTHER: \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**